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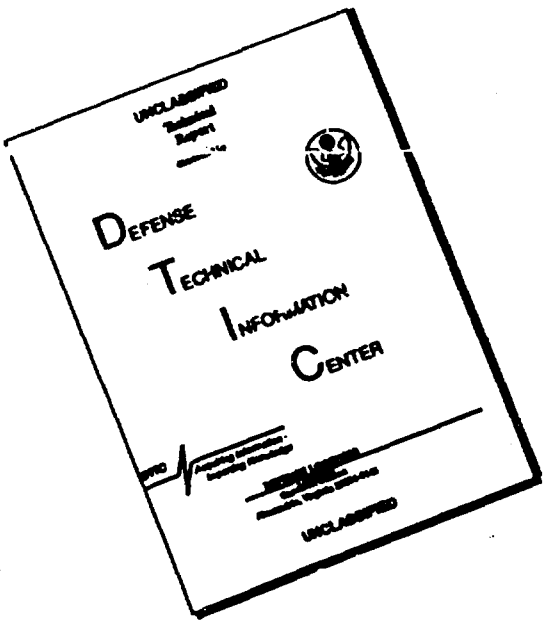

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Louse-Borne Relapsing Fever in Man

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Six Ethiopians with louse-borne relapsing fever died suddenly 4 to 12 hours after being treated with antibiotics. Autopsies demonstrated a diffuse myocarditis, hepatitis, and splenic microabscesses. The patients probably died of sudden myocardial failure during the hypotensive phase of the induced crisis. Autopsies on two additional patients with louse-borne relapsing fever, whose deaths appeared to be unrelated to the crisis, showed similar changes. We consider the myocarditis, hepatitis, and splenic microabscesses to be caused by a toxic component of the organism.

Louse-borne relapsing fever is a spirochetal infection caused by *Borrelia recurrentis*. Little has been published about the pathologic features of this disease despite the fact that pandemics with up to 70% mortality followed both World Wars.[1-3] Currently, an opportunity to study the disease exists in Ethiopia where more than 4,000 infections are reported annually.[4] In Ethiopia, death from the disease is often sudden, unexpected, and occurs shortly after the start of therapy. This report describes the postmortem findings in eight such patients and explores the possible mechanisms responsible for their deaths.

Methods

The diagnosis of relapsing fever was made in each patient by the demonstration of spirochetes in a smear of peripheral blood. The disorder was probably louse-borne because each patient was infested with body lice and resided in an area of Ethiopia where only the louse-borne type of disease has been reported.[5] Autopsies were performed on eight patients who died with the disorder. Tissues were fixed in formaldehyde solution (formalin) and duplicate sections were stained with hematoxylin-eosin, phosphotungstic acid-hematoxylin, Alcian blue, and a modified Warthin-Starry stain.

Report of Cases

CASE 1.—A 48-year-old man entered a provincial hospital with fever, abdominal pain, anorexia, and headache of unstated duration. He had a dry cough, a regular heart beat, and a temperature of 36.5 C (97.7 F). He was incontinent of stool and was semicomatose. He received 1 gm of tetracycline orally. Four and one-half hours after therapy was begun his temperature was 37 C (98.6 F) and the blood pressure was 80/50 mm Hg (previous levels were not recorded). He received 25 mg of prednisolone. The blood pressure continued to drop and was 75/40 mm Hg shortly before death. Seven and one-half hours after initial treatment the patient collapsed and died suddenly while returning to his bed from the lavatory.

CASE 2.—A 36-year-old man complained of fever, sweating, chills, and anorexia of several days duration. He had vomited frequently during the three days prior to admission and continued to vomit after admission. He was delirious and jaundiced. The blood pressure was 100/70 mm Hg. The chest roentgenogram revealed no abnormalities. The liver was moderately enlarged and the spleen was palpable at the left costal margin. An electrocardiogram recorded a pulse rate of 130 beats per minute, with a prolonged corrected Q-T interval and deviation of the right axis. The patient received 600,000 units of penicillin intramuscularly and 1 gm of tetracycline orally. Twelve hours after treatment began, the patient gasped for breath and died.

CASE 3.—A 35-year-old man entered a local hospital with a high fever of several days duration. His temperature was 39 C (102.2 F). Other clinical or laboratory findings were not recorded. He received 1 gm of tetracycline orally, in two doses, over a five-hour period. He collapsed and died nine hours after treatment began.

CASE 4.—A 23-year-old man complained of chills, headache, anorexia, weakness, and vomiting of six days duration. On admission to the hospital his temperature

Fig 1.—Interstitial edema and lymphocytic and plasmacytic infiltrate from left ventricle of heart (case 5) (hematoxylin-eosin, original magnification ×350). Inset, Abundant cardiac histiocytes in adjacent area of heart (hematoxylin-eosin, ×1,200).

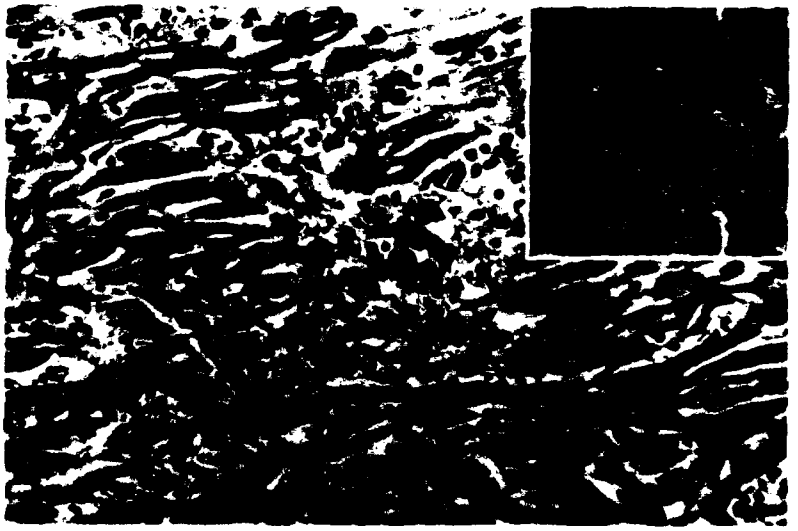

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Fig 2.—Microabscesses in spleen (case 4) appear as minute gray foci against dark background of cut surface of spleen (× 1).

Fig 3.—Splenic arterioles (arrows) with small intact cuffs of lymphocytes are surrounded by multiple irregularly shaped microabscesses (case 4) (hematoxylin-eosin, original magnification × 38).

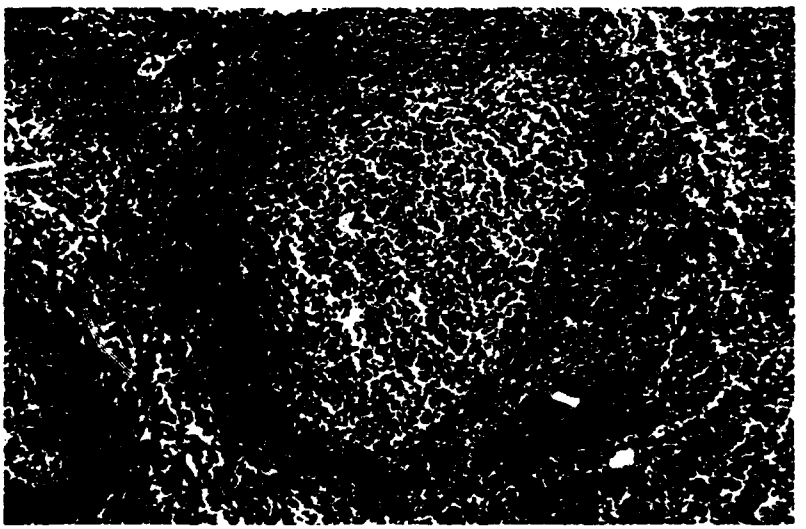


Fig 4.—Microabscesses of spleen with disintegrating leukocytes surrounded by thin rim of fibrin (case 4) (hematoxylin-eosin, original magnification × 150).

was 36.3 C (97.4 F), respirations were 38/min, and blood pressure was 94/50 mm Hg. The patient was deeply jaundiced and had hepatosplenomegaly. Laboratory studies disclosed the following values: hemoglobin, 11.2 gm/100 ml; white blood cell (WBC) count, 8,150/cu mm; blood urea nitrogen (BUN), 60 mg/100 ml; serum glutamic oxalic transaminase (SGOT), 20 Wroblewski units/ml; total serum bilirubin, 14.8 mg/100 ml (direct, 10.8 mg/100 ml); prothrombin time, 10% of the normal control; platelet count, 185,000/cu mm; partial thromboplastin time, 67 seconds; and plasma fibrinogen, 90 mg/100 ml. He had microspherocytes on a blood smear. The chest roentgenogram and serum electrolytes were normal. The electrocardiogram was abnormal, having a prolonged, corrected Q-T interval and inverted T waves in the anterior chest leads. The patient received 250 mg of tetracycline intravenously. His temperature rose to 39 C (102.2 F); pulse rate rose to 124 beats per minute; respiration rate to 58/min; and blood pressure to 152/86 mm Hg. Further data were not available, but the patient appeared to be improving when, seven hours following treatment, he died suddenly. Attempts at resuscitation failed.

Case 5.—A 14-year-old boy came to a local hospital with fever and delirium. The history of his illness could not be obtained, and the physical findings were not recorded. He received 1 gm of tetracycline orally. About eight hours later he died suddenly.

Case 6.—A 24-year-old man entered a provincial hospital with complaints of malaise, fever, backache, headache, and arthralgia of unstated duration. He had abdominal guarding, a cough, and a temperature of 41.4 C (106.6 F). No laboratory or other physical findings were recorded. Initial treatment included 400,000 units of penicillin G procaine, aspirin, and sponge baths. The following day his temperature had fallen to 36 C (96.8 F). Without further treatment his fever again rose to 39.5 C (103.1 F) on the third day of hospitalization. At that time he received 800,000 units of penicillin G procaine. Four hours later he suddenly began to gasp for breath and died.

Case 7.—A 24-year-old man entered a local hospital with a five-day history of chills, fever, malaise, myalgia, headache, and weakness. He was a small man with a dulled sensorium, a temperature of 37.5 C (99.5 F), a liver edge palpable 2 cm below the costal margin, jaundice, a blood pressure of 106/60 mm Hg, a pulse rate of 90 beats per minute, and a prolonged, corrected Q-T interval on electrocardiogram. Laboratory studies disclosed the following values: WBC count, 28,500/cu mm; hemoglobin, 11.3 mg/100 ml; BUN, 148 mg/100 ml; total serum bilirubin, 32.8 mg/100 ml (direct 18.2 mg/100 ml); SGOT, 300 Wroblewski units/ml; serum alkaline phosphatase, 7.3 Bessey-Lowry-Brock units/100 ml; prothrombin time, 42 seconds (control,

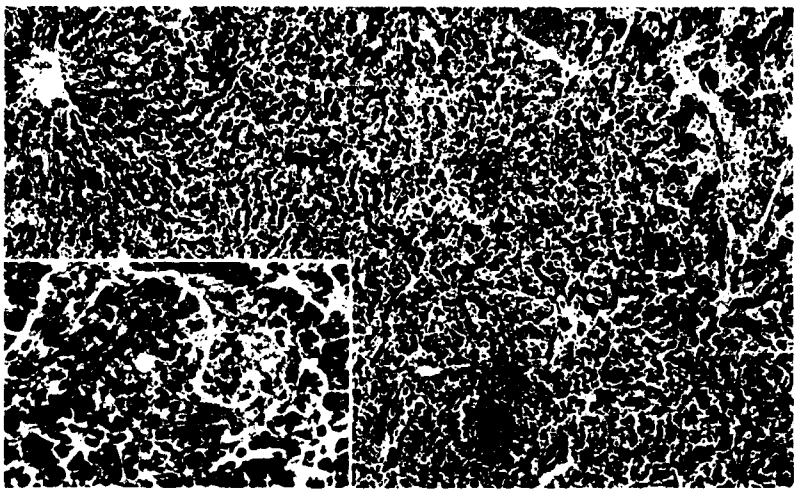


Fig 5.—Discrete foci of hemorrhage and necrosis in mid-zonal area of liver (case 4, hematoxylin-eosin, original magnification × 90). Inset, Detailed view of a focus (hematoxylin-eosin, × 350).

17.5 seconds); partial thromboplastin generation time, 79 seconds; platelet count, 63,000/cu mm; and fibrinogen, 410 mg/100 ml. He received 250 mg of tetracycline orally four times a day for two days. He passed through the crisis phase uneventfully, but his condition steadily deteriorated. He went into hepatic coma four days after the institution of therapy, when the following values of blood constituents were noted: hemoglobin, 10.25 mg/100 ml, BUN, 99 mg/100 ml, total serum bilirubin, 32 mg/100 ml (direct 21 mg/100 ml); SGOT, 1,050 Wroblewski units/ml; serum alkaline phosphatase, 10.64 Bessey-Lowry-Brock units/ml, prothrombin time, 20 seconds (control, 14 seconds); partial thromboplastin generation time, 53 seconds; platelet count, 86,000/cu mm; and fibrinogen, 415 mg/100 ml. He had a temperature of 36.5 C (97.7 F), deepening jaundice, a palpable spleen, and a blood pressure of 90/65 mm Hg. He died quietly the following day.

CASE 8.—A boy between 15 and 17 years old was admitted to a provincial hospital, unconscious and near death. He had "absent eye reflexes," a temperature of 36 C (96.8 F), rales over the left lung field, no jaundice, and a liver and spleen palpable 4 cm and 2 cm respectively below the costal margin. The patient was treated with 1 million units of penicillin and 1 gm of streptomycin. He died 30 minutes later, without showing signs of developing a crisis.

Postmortem Findings

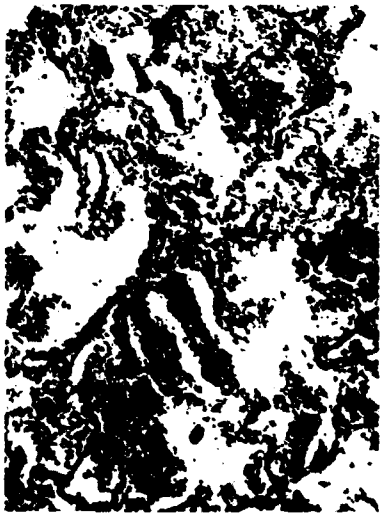
Gross findings at autopsy were fairly similar from case to case. Numerous petechial hemorrhages were present over the surfaces of the meninges, pleura, heart, kidneys, and mesentery. Hearts were near normal in size and had a diffuse, histiocytic interstitial myocarditis, most prominent about small arteries of the left ventricle and IV septum (Fig 1). Anitschkow myocytes and interstitial edema were prominent, the latter containing acid mucopolysaccharides by Alcian blue staining. No necrosis of either blood vessels or myocardial fibers was visible. The rare microhemorrhages visible in 5 hearts may have reflected small artery or arteriolar damage since many such vessels had swelling of endothelial cells. A few interstitial lymphocytes and plasma cells were present in all hearts but they were plentiful in case 7. Spirochetes were visible in blood vessels in case 8.

Spleens were firm and enlarged in all cases; the organs contained scat-

Fig 6.—Spirochetes are present in large numbers in proteinaceous cast despite "adequate therapy" four days before (case 7) (silver impregnation of Warthin-Starry, original magnification × 720).

Fig 7.—Small fibrin thrombus in adrenal sinusoid and perivascular deposition of fibrin (case 5) (Mallory phosphotungstic acid-hematoxylin, original magnification × 350).

Fig 8.—Intra-alveolar hemorrhage in lung (case 2) (hematoxylin-eosin, original magnification × 150).



Body Weight (kg) and Organ Weights (gm)							
Patient	Body Weight*	Heart	Lungs	Kidneys	Liver	Spleen	Brain
1	70	normal*	normal*	normal*	enlarged*	enlarged*	normal*
2	70	400	1,150	400	2,050	900	1,395
3	60	350	1,600	450	2,500	900	...
4	...	272	1,061	440	2,200	547	1,405
5	50	250	650	250	1,500	525	1,400
6	50	normal*	normal*	normal*	enlarged*	enlarged*	...
7	40	125	350	175	1,550	400	1,045
8	60	normal*	heavy*	normal*	enlarged*	enlarged*	...

* Estimated since no scale available.

tered, 2 to 10 mm irregularly shaped foci of gray tissue (Table, Fig 2). Histologically, the gray foci proved to be areas of necrosis that entirely replaced the white pulp (Fig 3 and 4). Filaments, compatible with fragmented spirochetes, were present in the foci of necrosis in case 8.

All livers were enlarged, mainly due to diffuse red blood cell (RBC) congestion and edema. Some liver cell cords were disrupted in all cases and mid-zonal regions often contained small, scattered foci of necrosis and hemorrhage (Fig 5). These lesions were most severe in the two patients with elevated SGOT levels. In these latter two patients, sinusoids contained many neutrophils and Kupffer cells were enlarged and numerous. The tissues from all patients who were jaundiced were bile-stained; intracanalicular bile stasis was present only in case 8. Spirochetes were present in vessels and sinusoids of the liver in case 8.

The kidneys were congested with occasional proteinaceous and RBC casts in collecting tubules and fibrin thrombi in a few glomerular capillaries. Spirochetes were present in the casts of five patients including one individual who died four days after the start of treatment (Fig 6). Intravascular spirochetes were numerous in patient 8. The adrenals were grossly normal with no hemorrhage or necrosis. A few cortical sinusoids contained fibrin thrombi, and fibrin surrounded occasional adventitial vessels (Fig 7).

All lungs contained focal intra-alveolar hemorrhages of varying size (Fig 8) and spirochetes were again demonstrated in the blood vessels in case 8. Only one patient, 7, had pancreatic abnormalities, a focal pancreatitis with bland fat necrosis. tiocytes, polymorphonuclear leukocytes, and lymphoblasts filled the dilated medullary cords of lymph nodes, which were usually enlarged. Cortical areas of the nodes showed diffuse blast transformation but no distinct germinal centers.

The five brains available for examination were mildly edematous, as evidenced by slight tentorial grooving and cerebellar coning. All were markedly congested, and in patient 5 there was a meningeal hemorrhage over the left occipital lobe which extended around vessels into the superficial cortex. Small hemorrhages surrounded an occasional vessel in patient 2; there was no cellular reaction to these hemorrhages.

Comment

Myocarditis is probably the commonest cause of death in fatal cases of relapsing fever.[6-12] Each of our patients had such a myocarditis and electrocardiographic evidence of a conduction defect was present in all three of the patients in which such records were taken as well as in many previously reported patients.[6,7] The myocarditis can apparently precipitate cardiac arrhythmias, which lead to sudden death.[8] This event would explain the sudden death of six of our eight patients.

It is well known that relapsing fever resolves by crisis, either spontaneously or about an hour after the first administration of an appropriate antibiotic.[7,13-25] The crisis is usually characterized by the abrupt onset of rigors; vasoconstriction; increase in body temperature, respiratory rate, heart rate, cardiac output, and systemic arterial pressure. Neutrophils degranulate, vacuolate, and markedly decrease in number in the peripheral blood. A respiratory alkalosis often appears. This initial phase of the crisis usually lasts 10 to 30 minutes and is followed by sustained hypotension with vasodilation and flushing; both cardiac output and pulse rate remain elevated.[26,27] Body temperature continues to rise and the WBC count continues to drop until the spirochetes disappear about two hours after the drug is first administered. By this time a metabolic acidosis has usually developed. Defervescence and recovery then commence as the various findings return toward normal. However, the systolic blood pressure may remain severely depressed for 8 to 12 hours with increases in central venous pressure accompanied by a prolonged but corrected Q-T interval and a gallop rhythm.[28] The aforementioned series of severe physiologic abnormalities no doubt stresses the damaged myocardium of patients with relapsing fever. This explains why death so often occurs during the crisis or during the period of circulatory collapse that immediately follows.[7,19,21,23-25,29-31]

Other findings reported in earlier publications were also present in the current study. Foci of necrosis that replace the nodular white pulp of the spleen have often been reported in the disorder.[12,24,31-38] Gross infarcts of the spleen, which were present in one of our patients, have often been observed in epidemics.[1,24,31,39] Splenic infarcts may also occur in relapsing fever complicated by infections with other septic agents.[12] Hepatic damage has been noted frequently in earlier reports.[7,23,24,28,39-41] Our findings of mid-zonal lesions in the hepatic lobule

corroborates a previous report.[12] Hepatic failure caused the death of one of our patients and has been previously reported in the later stages of infections.[12,24] Cerebral edema and hemorrhage were not severe enough in any of our patients to have directly caused death. Massive infarction of the cortex, meningitis, and intracerebral hemorrhage have been occasionally reported as a cause of death in the disease.[12,31,40]

There is some evidence that disseminated intravascular coagulation occurs in relapsing fever.[28,42,47] One of our patients exhibited a consistently depressed plasma fibrogen level, minimal depressed platelet count, microspherocytes in the blood, petechiae on serosal surfaces, bleeding in viscera, and irreversible shock. This patient and four others had a few scattered fibrin thrombi in small vessels. Hemorrhage has frequently been reported in relapsing fever.[3,7,9,10,12,22-25,31,40-44] There is usually a petechial skin rash or epistaxis. Occasionally, hemorrhage has caused death, usually secondary to a ruptured spleen.[25] No instances of gangrene, renal cortical necrosis, or adrenal necrosis have been reported.

The presence of spirochetes in renal casts in one of our patients is of particular interest since antibiotic treatment had been completed three days earlier. Similar casts without spirochetes were present in four other patients. Spirochetes in casts may be partially protected from antibiotics, and therefore, serve as one possible source of the reinfections that sometimes develop.

It is desirable to suggest but difficult to prove a unifying theory for the pathogenesis of the varied lesions of louse-borne relapsing fever. Data from humans (case 8) and animals[45] indicate that the lesions in the hearts, livers, and spleens are present prior to the crisis and suggest a specific toxic effect of the organism or its products (D. M. Judge, MD; J. LaCroix, MD; P. L. Perine, MD, unpublished data). The number of circulating organisms is usually so large, some patients have greater than 100,000/cu mm of blood,[28] that substances with mild toxicity could have an important effect. The similarity between the crisis and endotoxin shock suggests that there is an endotoxin in *B recurrentis*.

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References

1. Le Gac P: L'Epidemie de Fievre Recurrente. *Ann Med Pharm Colon* 29:148-165, 1931.

2. Maurice GK, cited by Kirk R: The epidemiology of relapsing fever in the Anglo-Egyptian Sudan. *Ann Trop Med Parasitol* 33:125-140, 1939.

3. Beveridge CEG: The louse-borne type of relapsing fever as prevalent in the Anglo-Egyptian Sudan, 1926 and 1927. *Med J Aust* 1:110-112, 1928.

4. *Weekly Epidemic Record. WHO* 45:261, 1970.

5. Sparrow H: The relapsing fevers, in *Tropical Health: A Report on a Study of Needs and Resources*. Washington, DC, National Research Council, Division of Medical Sciences, 1962, pp 499-500.

6. Vukotic D: Clinical and electrocardiographic findings of the heart in patients with louse-borne relapsing fever at the "Day of Crisis" and seven days later. *Ethiopian Med J* 6:167-170, 1958.

7. Chung HL, Chung FC: Relapsing fever: Clinical and statistical study of 337 cases. *Chinese Med J* 55:6-33, 1939.

8. Parry EHO, et al: Some effects of louse-borne relapsing fever on the function of the heart. *Am J Med* 49:472-479, 1970.

9. Robinson P: Relapsing fever in Addis Ababa. *Br Med J* 2:216-217, 1942.

10. Belezky WK, Umanskaja RM: Die Recurrensspirochatise des zentralen Nervensystems des Menschen. *Z Ges Neurol Psychiatr* 129:21-41, 1930.

11. Gore I, Saphir O: Myocarditis: A classification of 1402 cases. *Am Heart J* 34:827-830, 1947.

12. Anderson TR, Zimmerman LE: Relapsing fever in Korea: A clinicopathologic study of eleven fatal cases with special attention to association with Salmonella infections. *Am J Pathol* 31:1038-1109, 1955.

13. Armand-Delille P, Lemaire G, Lemaire H: Les principaux caracteres de la fievra recurrente observee a l'armee d'orient. *Bull Soc Med Hosp Paris* 41:778-780, 1917.

14. Calwell WK: Relapsing fever: An account of a series of 125 cases, with special reference to the Palestine type. *Lancet* 2:785-788, 1920.

15. Calero C: Relapsing fever on the Isthmus of Panama: Report of 106 cases. *Am J Trop Med Hyg* 26:761-769, 1946.

16. Garnham PCC, et al: An epidemic of louse-borne relapsing fever in Kenya. *Trans R Soc Trop Med Hyg* 41:141-170, 1947.

17. Harrison IB, Whittington RM: Antibiotics in the treatment of relapsing fever. *US Armed Forces Med J* 2:1859-1862, 1951.

18. Juarez E: Nueva aportacion al tratamiento de la fiebre recurrente espanola con aureomicina. *Rev Sanid Hig Publica* 30:489-498, 1956.

19. Kamal AM, Messih GA: Louse-borne relapsing fever (clinical signs and symptoms). *J Egypt Public Health Assoc* 22:23-30, 1947.

20. Ling C: A preliminary study of the treatment of Chinese louse-borne relapsing fever with penicillin. *Chinese Med J* 6:225-230, 1947.

21. McCulloch WE: Relapsing fever in Northern Nigeria: A study of 300 cases. *J Trop Med Hyg* 28:332-341, 1925.

22. Robertson RC: Relapsing fever in Shanghai. *Chinese Med J* 66:854-885, 1932.

23. Roy SC: Relapsing fever epidemic in Seoni district (Central Provinces), February to May, 1920. *Indian Med Gaz* 56:7-9, 1921.

24. Russell H: Human and experimental relapsing fever, Accra, Gold Coast, 1929-1930. *West Afr Med J* 4:59-66, 1931.

25. Wolff BP: Asiatic relapsing fever: Report of 134 cases treated with Mapharsen. *Ann Intern Med* 24:203-216, 1946.

26. Parry EHO, Bryceson ADM, Leithead CS: Acute haemodynamic changes during treatment of louse-borne relapsing fever. *Lancet* 1:81-83, 1965.

27. Schofield TPC, et al: Leukopenia and fever in the "Jarisch-Herxheimer" reaction of louse-borne relapsing fever. *Lancet* 1:58-62, 1968.

28. Bryceson ADM, et al: Louse-borne relapsing fever, a clinical and laboratory study of 62 cases in Ethiopia and reconsideration of the literature. *Q J Med* 39:129-170, 1970.

29. Ordman D: Relapsing fever in Africa. *Cent Afr J Med* 3:347-356, 1957.

30. Balteanu I, Russ M, Voiculescu M: Les proprietes spirochetolytoques de serum de convalescent de fievre recurrente. *Arch Roum Pathol Exp Microbiol* 15:310-312, 1948.

31. El Ramly AH: Three papers on louse-borne relapsing fever. *J Egypt Public Health Assoc* 21:125-182, 1946.

32. Belezky WK, Umanskaja RM: Über die Natur der Immunitat bei Ruckfallfieber. *Virchow Arch Pathol Anat* 272:305-312, 1929.

33. Cleland JB: A death from relapsing fever in Australia. *Med J Aust* 1:820-821, 1938.

34. Kulescha GS, Titowa NA: Die pathologische Anatomie und Atiologie der Komplikationen des Ruckfallfiebers. *Virchow Arch Pathol Anat* 241:319-351, 1923.

35. Lubimoff N: Ueber die pathologisch-anatomischen Veranderungen bei Typhus biliosus. *Virchow Arch Pathol Anat* 98:160-192, 1884.

36. Nasu T: Pathological studies in relapsing fever. *Trans Soc Pathol Jap* 38:377-379, 1949.

37. Nikiforoff M: Zur pathologischen Histologie der Milz bei Recurrens. *Beitr Pathol* 12:206-221, 1893.

38. Russell H: The pathology of the spleen in replapsing fever. *Trans R Soc Trop Med Hyg* 26:259-265, 1932.

39. Legerton CW, Chambers WL: Spontaneous rupture of the spleen in relapsing fever. *US Armed Forces Med J* 1:88-90, 1950.

40. Babes V: Hemorragies meningees et autres manifestations hemorragiques dans la fievre recurrente. *CR Soc Biol* 79:855-857, 1916.

41. Benhamou E: Aspects actuels de la fievre recurrente epidemique en Afrique de Nord. *Bull Acad Natl Med* 129:530-532, 1945.

42. Chu FT, Derrick S, Chung SF: Relapsing fever in children. A study of 26 epidemic cases. *Nat Med J China* 17:224-232, 1931.

43. Perine PL, et al: Bleeding in louse-borne relapsing fever: II. Fibrinolysis following treatment. *Trans R Soc Trop Med Hyg* 65:782-787, 1971.

44. Willcox WH: Typhus and relapsing fever in Mesopotamia and Northern Persia. *Proc R Soc Med* 13:59-182, 1946.

45. Judge DM, Perine PL: On the pathology of louse-borne relapsing fever, abstracted [illegible] before the eighth International Congresses on Tropical Medicine and Malaria, Tehran, Iran, 1968.

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